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Cancer Prevention Research

Research Article

Combined Lifestyle Factors and Risk of Incident Colorectal Cancer in a Chinese Population

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Abstract

A body of research links dietary intake, alcohol consumption, smoking, physical activity, body mass index (BMI), and possibly sleep patterns with colorectal cancer risk. However, little research has examined the association of the combination of these lifestyle factors with incidence of colorectal cancer, especially in non-Western populations. A protective lifestyle factor index of these six aforementioned factors was created and examined in relation to risk of developing colorectal cancer. This study is a prospective observational study of 50,466 Chinese men and women in Singapore ages 45 to 74 years during enrollment in the Singapore Chinese Health Study in 1993–1998 and followed up through 2007. The main outcome measures were standardized rates and HRs of incident colorectal cancer. The protective levels of each lifestyle factor were independently associated with reduced age- and sex-standardized incidence rates of colon cancer. When all the factors were combined into a single protective lifestyle factor index, there was a strong, monotonic decrease in incidence rate of colon cancer with an increasing score. Relative to participants with an index score of 0 to 3, the HRs (95% confidence intervals) of colon cancer for an index score of 4, 5, 6, 7, 8, and 9/10 were 0.58 (0.35–0.95), 0.56 (0.36–0.86), 0.50 (0.33–0.76), 0.43 (0.28–0.66), 0.39 (0.25–0.63), and 0.25 (0.12–0.54; $P_{trend} < 0.0001$). The results were consistent by sex. Conversely, there was no association with rectal cancer risk. An increasing protective lifestyle factor index score is associated with a marked decreased risk of developing colon cancer in Chinese men and women. *Cancer Prev Res; 6(4); 360–7. ©2012 AACR.*

Introduction

On the global level, colorectal cancer is the third most common cancer in men and second most common in women (1). In Chinese Singaporeans, colorectal cancer is the most common cancer in men and second most common in women with rates among the highest globally (2, 3). However, these high rates are not the historical norm as they stem from the doubling in age-standardized rates between 1968 and 1997 (4, 5). This overall increase in colorectal cancer rates in the past four decades is primarily due to the increasing incidence of colon cancer (3, 5). This trend corresponds with the rapid economic development and concomitant shifts from a traditional lifestyle toward a Westernized lifestyle and increased life expectancy since the country became independent in 1965 (6, 7).

Evidence suggests that lifestyle factors including dietary intake, alcohol consumption, cigarette smoking, physical activity, body mass index (BMI), and more recently sleep are all associated with risk of colorectal cancer (8–11). Colon cancer has ties to all these factors, whereas the evidence for rectal cancer is inconsistent (9, 12, 13). These data suggest preventive potential of these cancers. However, few studies have examined the association between combined lifestyle factors and the risk of developing colorectal cancer (14, 15) and none in a non-Western population.

Using the Singapore Chinese Health Study, a population-based longitudinal cohort of Chinese men and women, we created a protective lifestyle factor index composed of a dietary pattern, physical activity, alcohol intake, sleep habits, smoking status, and BMI and examined the association of this index with incident colorectal cancer.

Materials and Methods

Study population

The design of the Singapore Chinese Health Study has been described previously (16). Briefly, the cohort was drawn from men and women, ages 45 to 74 years, who belonged to one of the major dialect groups (Hokkien or Cantonese) of Chinese in Singapore. Between April 1993 and December 1998, 63,257 individuals completed an

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in-person interview that included questions on usual diet, demographics, height and weight, use of tobacco, usual physical activity, menstrual and reproductive history (women only), medical history, and family history of cancer. The Institutional Review Boards at the National University of Singapore (Singapore, Singapore), University of Pittsburgh (Pittsburgh, PA), and the University of Minnesota (Minneapolis, MN) approved this study.

Assessment of lifestyle risk factors

At the baseline interview, all lifestyle factors were collected by self-report. BMI (kg/m^2) was calculated from height and weight. Inquiry on smoking habits included smoking status (never, former, or current smoker) and former and current (i.e., ever) smokers were further asked for age at starting or quitting smoking, number of cigarettes per day, and number of years of smoking (17). Physical activity was assessed using 8 continuous categories ranging from never to 31 hours or more in an average week spent doing strenuous sports (e.g., jogging, bicycling on hills, tennis, squash, swimming laps, or aerobics), vigorous work (e.g., moving heavy furniture, loading or unloading trucks, shoveling, or equivalent manual labor), and moderate activities (e.g., brisk walking, bowling, bicycling on level ground, tai chi, and chi kung). Usual sleep duration was assessed by the following question: "On average, during the last year, how many hours in a day did you sleep?", with response categories of 5 hours or less, 6, 7, 8, 9, and 10 or more hours. For each of the 4 types of alcoholic beverages (beer, wine, Western hard liquor, and Chinese hard liquor), participants were asked to choose from 8 frequency categories: never or hardly, once a month, 2–3 times a month, once a week, 2–3 times a week, 4–6 times a week, once a day, and 2 or more times a day. Consumers were then asked to choose from 4 defined portion sizes. For beer, the portion sizes were one small bottle (375 mL) or less, 2 small bottles or 1 large bottle (750 mL), 2 large bottles, and 3 large bottles or more. For wine, the portion sizes were 1 glass (118 mL) or less, 2, 3, and 4 glasses or more. For Chinese or Western hard liquor, the portion sizes were 1 shot (30 mL) or less, 2, 3, and 4 shots or more. One drink was defined as 375 mL of beer (13.6 g of ethanol), 118 mL of wine (11.7 g of ethanol), and 30 mL of Western or Chinese hard liquor (10.9 g of ethanol). We expressed levels of alcohol intake in units of "drinks" per week to facilitate comparison with Western populations (18). Dietary intake was assessed with a semi-quantitative food frequency questionnaire (FFQ) specifically developed for this population encompassing 165 commonly consumed food items. The questionnaire has been validated (16, 19, 20). Dietary patterns were derived using principal component analysis (PCA) including all 165 foods and beverages (besides alcohol) using methods described previously (21). The aim of PCA in nutritional analyses is to account for the maximal variance of dietary intake by combining the many different dietary variables into a smaller number of factors based upon the intercorrelation of these variables. A vegetable, fruit, and soy rich pattern was included. The pattern is characterized by high correlation and intake of those respective foods with a higher pattern score and lower intake of meats, dimsum, Western-style fastfood, and sugared soft drinks.

Classification of protective lifestyle factors

Lifestyle factors were characterized as protective based upon their independent association with colon cancer, or in the case of smoking, the greater body of evidence and public health recommendations (8). There was no evidence that any factors except smoking and alcohol intake were associated with risk of rectal cancer. Previously published work examining BMI, smoking, and alcohol with colorectal cancer risk in the cohort guided characterization of these factors (18, 22). Cigarette smoking was classified into never smoker, light, and heavy smoker (18). The "heavy" smokers were those who started to smoke before 15 years of age and smoked 13 or more cigarettes per day; all remaining ever smokers were defined as light smokers. For the dietary pattern, we updated the analysis to include all nonalcoholic foods and beverages compared with the simplified approach previously published (23). The protective definition of dietary intake in the cohort was based on ranking of the vegetable, fruit, and soy-rich dietary pattern score. For the other lifestyle factors, protective levels were also based on the data from the Singapore cohort generally aligning with the literature base on the topic. Strenuous activity or vigorous work was categorized as $\geq$1.5 versus <1.5 hours/wk. Moderate physical activity was not associated with colon cancer risk. A protective level of sleep was categorized as 6 to 8 h/d versus $\leq$5 or $\geq$9 h/d. Each lifestyle factor was coded as 1 or 2 for being protective depending on a threshold or tiered association, as well as the magnitude of associated risk, and 0 for the referent.

Case ascertainment

Identification of incident colorectal cancer cases and deaths occurred through record linkage analysis of the cohort database with the population-based Singapore Cancer Registry and the Singapore Registry of Births and Deaths. The nationwide cancer registry has been in place since 1968 and has been shown to be comprehensive in its recording of cancer cases (4). As of April 2008, only 27 cases were known to be lost to follow-up due to migration out of Singapore. As of December 31, 2007, 969 participants included in this study had developed invasive colorectal cancer (590 colon cancers and 379 rectal cancers). In the analysis, rectal cancers included cancers of the rectosigmoid junction. Of the colorectal cancer cases, 97% were confirmed histologically (n = 940) and the remaining cases were diagnosed clinically (n = 23) or identified through death certificates (n = 6).

Statistical analysis

We excluded 1,936 of the original 63,257 participants with a history of invasive cancer (except non-melanoma skin cancer) or superficial, papillary bladder cancer at baseline as they did not meet study inclusion criteria, plus another 10,070 participants missing either or both height and weight measures. Participants excluded because of

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missing BMI (N = 10,070) were not materially different across the noted demographic and lifestyle characteristics compared with participants with full data who were included in the analysis. We also excluded 785 additional participants who reported extreme sex-specific energy intakes (<600 or >3,000 kcal women) (<700 or >3,700 kcal men). The present analyses included 50,466 participants.

For each study subject, person-years were counted from the date of baseline interview to the date of cancer diagnosis, the date of death, date of last contact (for the few subjects who migrated out of Singapore) or December 31, 2007, whichever occurred first. Age- and sex-standardized cancer rates were calculated using the person-year weight of the entire cohort.

Proportional hazards (Cox) regression methods were used to examine the associations between the individual and combined protective lifestyle factors and hazard risk of developing colorectal cancer. We estimated the HR of colorectal cancer and the corresponding 95% confidence interval (CI). There was no evidence that proportional hazards assumptions were violated.

In the analysis considering individual lifestyle factors and BMI, the model included all the individual factors simultaneously, as well as age (<50, 50–54, 55–59, 60–64, 65+), sex, year of interview (1993–95 and 1996–98), dialect (Hokkien vs. Cantonese), level of education (no formal schooling, primary school, secondary school or above), baseline physician diagnosed diabetes mellitus (yes vs. no), first-degree familial history of colorectal cancer (yes vs. no), and total energy intake (kcal/d).

The same adjustments were made in the analysis of the protective lifestyle factor index in relation to colorectal cancer risk. The protective lifestyle factor index was the sum of the protective score of 1 or 2 over all 5 lifestyle factors and BMI dependent on the level of a given variable (see the coding scheme in Table 1). Participants could score from 0 to 10 with a score of 0 equating to no protective lifestyle factors and 10 equating to the protective level of each factor. Tests for trend were conducted by entering the index score into the model as a continuous variable.

Effect modification of the associations was considered by age, sex, and educational attainment. To reduce potential bias due to patients with underlying disease at enrollment, we conducted parallel sensitivity analyses after excluding all cohort participants with diabetes at baseline as well as excluding all person-years and colorectal cancer cases that occurred within the first 3 years post enrollment. Finally, we examined the association by proximal versus distal colon cancer and localized versus advanced cancer as determined by the Dukes staging system (A and B vs. C and D). All regression analyses were conducted using SAS statistical software version 9.2 (SAS Institute). All P values quoted are 2-sided.

Results

During 579,628 person-years of follow-up, there were 969 incident cases of colorectal cancer, of which 590 (61%) were colon cancer. The definition of, and association of, 5 different independent lifestyle factors and BMI with risk of developing colon cancer are presented in Table 1. The protective level of each individual factor was associated with a lower age- and sex-standardized rate of colon cancer. Despite lower rates of colon cancer in light and never-smokers, adjusted HRs for colon cancer were comparable

Table 1. Individual lifestyle factors and their independent association with risk of colon cancer: the Singapore Chinese Health Study

Lifestyle factor (index score)	%	Rate[a]	HR (95% CI)
BMI, kg/m^2			
<18.5 or ≥27.5 (0)	17.9	127	1.00
18.5–27.4 (1)	82.1	96	0.79 (0.65–0.96)
Alcohol intake, drinks/wk			
>14 (0)	2.3	187	1.00
8–14 (1)	2.3	147	0.73 (0.40–1.33)
0–7 (2)	95.4	99	0.51 (0.33–0.78)
Cigarette smoking[b]			
Heavy smokers (0)	3.6	140	1.00
Light smokers (1)	26.6	121	0.96 (0.64–1.44)
Never smokers (2)	69.8	93	1.12 (0.74–1.69)
Dietary pattern score[c]			
Lowest 25th percentile (0)	25.0	125	1.00
Middle 50th percentile (1)	50.0	101	0.88 (0.72–1.06)
Highest 25th percentile (2)	25.0	81	0.76 (0.59–0.98)
Physical activity, h/wk[d]			
<1.5 (0)	90.1	107	1.00
≥1.5 (2)	9.9	53	0.61 (0.42–0.88)
Sleep, h/d			
<6 or ≥9 (0)	15.9	137	1.00
6–8 (1)	84.1	95	0.82 (0.67–1.00)

Model includes all factors simultaneously and adjusted for age, sex, dialect, year enrolled, education, diabetes status, familial history of colorectal cancer, and energy intake.

[a]Rate = age- and sex-standardized incident rate of colon cancer per 100,000 person-years using person-year time, age and sex distributions of Singapore Chinese Health Study (SCHS).

[b]Cigarette smoking: The "heavy" smokers were those who started to smoke before 15 years of age and smoked 13 or more cigarettes/d; all remaining ever smokers were defined as light smokers.

[c]Dietary pattern score: an increasing score in the vegetable/fruit/soy pattern is characterized by higher intake of vegetables, fruit, and soy and lower intake of meats, dimsum, Western-style fastfood, and sugared soft drinks.

[d]Physical activity represents amount of strenuous physical activity and/or vigorous work.

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Table 2. Baseline participant characteristics according to protective lifestyle factor index

Protective lifestyle factor index score	0/1/2/3	4	5	6	7	8	9/10
N	1,035	2,541	7,127	13,677	16,463	7,480	2,143
Age	57.2 (7.7)	58.2 (8.2)	57.8 (8.1)	56.6 (8.0)	55.3 (7.7)	54.4 (7.4)	52.1 (6.2)
Sex (% female)	9.3	21.6	37.4	55.1	66.9	65.2	33.8
Education, %	21.4	22.5	25.7	28.9	32.7	38.1	53.4
Diabetes, %	8.3	9.2	10.6	9.7	8.4	7.3	5.6
BMI, kg/m^2	22.2 (4.9)	22.9 (4.9)	23.4 (4.5)	23.3 (3.8)	23.0 (3.0)	22.9 (2.4)	23.0 (2.5)
Percent reporting protective level of lifestyle factor							
BMI	48.6	53.7	65.0	77.6	91.3	97.3	96.2
Dietary pattern[a]	20.3	24.2	36.2	57.7	73.1	11.2	50.0
Dietary pattern[b]	0.9	2.5	3.5	8.5	23.5	83.0	50.0
Physical activity	1.0	1.8	1.7	2.5	5.7	18.5	100.0
Sleep	49.4	57.4	68.5	80.9	92.3	97.3	95.9
Smoking[c]	60.1	62.9	56.5	31.2	12.8	7.5	11.2
Smoking[d]	2.9	13.9	36.7	66.9	86.7	92.3	88.8
Alcohol intake[e]	11.1	10.2	4.4	2.0	0.8	0.5	0.5
Alcohol intake[f]	35.5	77.8	92.9	97.4	99.0	99.4	99.5

NOTE: Data for age and BMI represent mean (SD). Education- percentage with secondary school level or higher.
[a]Middle 50th percentile (25–75th) of dietary pattern score.
[b]Upper 25th percentile of dietary pattern score.
[c]Light.
[d]Never.
[e]8–14 drinks/wk.
[f]0–7 drinks/wk.

across different smoking categories. Every other lifestyle factor displayed an independent association with risk of colon cancer. In line with previous published results (18, 22, 23), only alcohol and smoking were associated with rectal cancer risk (data not presented).

As the protective lifestyle factor index score increased, a greater proportion of participants was more educated and female except in the top lifestyle index score group (9 of 10 points) where the proportion of females decreased. Diabetes prevalence and BMI levels displayed a subtle inverse U-shape association, and mean age slightly declines with an increasing score (Table 2). Table 3 displays age- and sex-standardized rates and HRs with 95% CIs for incident colon, rectal and overall colorectal cancer according to the protective lifestyle factor index. A graded decrease in age- and sex-standardized rates of overall colorectal, colon, and rectal cancers was observed with an increasing protective lifestyle factor index score. In the Cox regression model, individuals with the highest score of 9 or 10 points had one-fourth the risk of developing colon cancer relative to those with the score of 0 to 3 (i.e., the poorest lifestyle). There was no association between an increasing protective lifestyle factor index score and risk of rectal cancer.

We conducted a sensitivity analysis examining the combined association of lifestyle factors in this cohort significantly associated with colon cancer (BMI, dietary pattern, sleep, physical activity, and alcohol) to determine how this approach affects the rates and risk estimates as smoking is not associated with colon cancer in the cohort (Supplementary Table S1). A stronger graded association for a decreased risk for colon cancer was observed with this approach; and this also emphasizes the null association between other lifestyle factors and rectal cancer.

Because there has been little prospective examination of sleep with colon cancer, a further sensitivity analysis examined whether sleep habits make an independent contribution to the lifestyle factor index. To address this, we created an index of BMI, the dietary pattern, physical activity, and alcohol intake with 7 possible protective lifestyle points. In the fully adjusted model, including adjustment for sleep and smoking habits, the results show that sleep does make an independent contribution to the point estimate. Relative to 0/1/2 points on the index, those with 3, 4, 5, and 6/7 points had a respective HR (95% CI), of 0.71 (0.53–0.94), 0.59 (0.45–0.78), 0.54 (0.39–0.75), and 0.28 (0.15–0.51). In the index including sleep (Supplementary Table S1), the HRs are 0.52, 0.42, 40, 31, and 20. Thus, removing sleep from the index attenuated the magnitude of the results showing an independent contribution of sleeping habits with colon cancer risk.

Because of different incidence rates of colorectal cancer and different prevalence of smoking habits and alcohol

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Table 3. Age- and sex-standardized incident colorectal cancer rates and HRs and 95% CIs of incident colorectal cancer according to a protective lifestyle factor index in Chinese men and women

Protective lifestyle factor index score	0/1/2/3	4	5	6	7	8	9/10	
N	1,035	2,541	7,127	13,677	16,463	7,480	2,143	
Colorectal cancer								
Cases (*n*)	40	62	185	278	280	102	22	P_{trend}
Standardized rate[a]	371	230	237	178	145	115	86	
HR (95% CI)	1.00	0.59 (0.39–0.87)	0.64 (0.45–0.91)	0.56 (0.40–0.78)	0.52 (0.37–0.73)	0.45 (0.31–0.65)	0.37 (0.22–0.62)	<0.0001
Colon cancer								
Cases (*n*)	26	41	110	175	166	62	10	P_{trend}
Standardized rate[a]	241	152	141	112	86	70	39	
HR (95% CI)	1.00	0.58 (0.35–0.95)	0.56 (0.36–0.86)	0.50 (0.33–0.76)	0.43 (0.28–0.66)	0.39 (0.25–0.63)	0.25 (0.12–0.54)	<0.0001
Rectal cancer								
Cases (*n*)	14	21	75	103	114	40	12	P_{trend}
Standardized rate[a]	130	78	96	66	59	45	47	
HR (95% CI)	1.00	0.59 (0.30–1.17)	0.81 (0.45–1.43)	0.66 (0.37–1.16)	0.69 (0.39–1.21)	0.55 (0.30–1.02)	0.57 (0.26–1.24)	0.11

NOTE: Model adjusted for age, sex, year of enrollment, dialect, education, diabetes status, familial history of colorectal cancer, and energy intake.

[a]Standardized rate = age- and sex-standardized incident cancer rate per 100,000 person-years using person-year time, age and sex distributions of Singapore Chinese Health Study (SCHS).

consumption between men and women in this population, we created a modified protective lifestyle factor index composed of the dietary pattern, physical activity, sleep, and BMI to provide better context for comparison between men and women. Results from this analysis are presented in Table 4 for colon cancer displaying the consistency of the association.

There was no evidence the results differed by age or education. Exclusion of participants with diabetes at baseline did not materially change the associations observed, nor did adjustment for hormone replacement (HRT) therapy in women or overall nonsteroidal anti-inflammatory drugs (NSAID) use. Of note, the nature of the results did not differ by subsite (proximal vs. distal) or stage (localized vs. advanced) of colon cancer (data not shown). A further sensitivity analysis for colon cancer displayed a stronger inverse association upon exclusion of data within the first 3 years of follow-up, suggesting that the association was

Table 4. Sex-stratified results—age-standardized incident rates and HRs and 95% CIs of incident colon cancer according to a modified protective lifestyle factor index (dietary pattern, physical activity, sleep, and BMI)

Protective lifestyle factor index score	0/1	2	3	4	5/6	P_{trend}
Women						
n cases/*N*	39/2,357	97/7,616	110/11,554	38/5,175	2/754	
Standardized rate[a]	79	62	49	34	6	
HR (95% CI)	1.00	0.80 (0.55–1.16)	0.65 (0.44–0.94)	0.55 (0.35–0.89)	0.25 (0.06–1.05)	0.002
Men						
n cases/*N*	45/2,176	83/6,371	121/7,835	44/4,430	11/2,198	
Standardized rate[a]	91	52	54	39	31	
HR (95% CI)	1.00	0.63 (0.44–0.91)	0.74 (0.52–1.05)	0.52 (0.34–0.80)	0.33 (0.17–0.66)	0.002
All						
n cases/*N*	84/4,533	180/13,987	231/19,389	82/9,605	13/2,952	
Standardized rate[a]	171	114	103	73	37	
HR (95% CI)	1.00	0.71 (0.55–0.92)	0.69 (0.54–0.89)	0.54 (0.39–0.74)	0.32 (0.17–0.57)	<0.0001

NOTE: Model adjusted for age, sex, year of enrollment, dialect, education, diabetes status, familial history of colorectal cancer, smoking, alcohol intake, and energy intake.

[a]Standardized rate = age-standardized incident cancer rate per 100,000 person-years using person-year time and age distributions of Singapore Chinese Health Study (SCHS).

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not due to underlying or undiagnosed cancers at baseline or otherwise poor health (data not shown).

Discussion

Chinese men and women with an increasing protective lifestyle factor index score represented by a dietary pattern emphasizing vegetables, fruit, and soy and lower in meats, dimsum, Western-style fastfood, and sugared soft drinks, higher relative levels of strenuous sports or vigorous work, zero to light alcohol consumption of not more than 7 drinks/wk, average usual sleep of 6 to 8 h/d, no history of smoking, and who were not underweight or obese were at a significantly reduced risk of developing colon cancer relative to their peers with either poor or nonadherence to these protective lifestyle factors. Exclusion of smoking from the index, a lifestyle factor not independently associated with colon cancer in the cohort, strengthened the results. The protective lifestyle factor index score was not associated with risk of developing rectal cancer.

Few studies have examined the combination of lifestyle factors with incident colorectal cancer. In a Danish cohort study, participants adhering to an increasing number of healthy lifestyle recommendations on physical activity, smoking, alcohol, certain dietary components, as well as waist circumference, experienced a stepwise decrease in risk of colon cancer during follow-up (14). Results were suggestively inverse but nonsignificant for rectal cancer. In the Health Professionals Follow-up Study, a risk score composed of BMI, physical inactivity, alcohol consumption, smoking habits, red meat consumption, and folic acid supplement use showed that an increasing risk score representing a poorer lifestyle was associated with increased risk of developing colon cancer (15).

A couple of other studies approached this topic in a different manner. In the Nurses' Health Study, both lifestyle and other factors were combined in an index (24). Relative risk was estimated on the basis of the cumulative incidence of colon cancer by the age of 70 years. In an analysis combining smoking, high BMI, low physical activity, high red/processed meat consumption, no screening, and low folate intake, the high-risk group was at a significant increased risk of developing colon cancer relative to the low-risk group. The Physician's Health Study found that a combination of increasing age, smoking, greater alcohol intake, and BMI significantly increased risk of colorectal cancer relative to low-risk values (25).

In summary, our study and these others each suggests that when lifestyle and other factors are considered in combination, a strong graded association with risk of colon cancer is observed, but a less clear association with rectal cancer is apparent. Each study is unique in its derivation and inclusion of factors, making comparability only suitable on a general level. Our study differs from the other studies in that we accounted for the overall dietary pattern instead of individual food items or nutrients, examined a Chinese population, and we also included sleep habits as a factor. There have been a limited number of studies on sleep patterns in relation to colorectal cancer risk, and our study raises the possibility that the duration of sleep may be an independent risk factor for colon cancer. This association is plausible as sleep deprivation may result in adverse physiologic changes in pathways relevant to colon cancer risk, such as disruption of circadian rhythm and related hormonal production (10), glucose and insulin pathways plus other metabolic defects (26) and inflammation (27). Furthermore, longer sleep duration may be representative of underlying inflammatory illness or disease (28) and may also further promote colon tumor multiplicity (11).

The exact mechanism whereby the noted combined lifestyle factors affect risk for colon cancer is unknown. The plausible biologic effects of each factor are pleiotropic in nature with likely overlapping influence on noted pathways thought to be relevant to colon cancer development, including insulin resistance and secretion, insulin-like growth factor (IGF)-I axis, other hormonal levels, and inflammation (9, 29, 30). The disparate results between colon and rectal cancers in the current study may stem from differences in the carcinogenesis of these 2 subsites. Our results suggest that although colon and rectal cancers share a general anatomic site, they seem to have different etiologic factors. Possible differences in etiology and development of colon and rectal cancer have been outlined in multiple avenues (12, 13).

Other evidence that colon cancer risk is largely attributable to lifestyle stems from the large difference in rates observed between highly and less developed populations (31). Related migration studies show populations that migrate from historically low- to high-risk countries begin mirroring the incidence trend of the new country (32). Moreover, while there is certainly a genetic component to the disease, it is estimated that 95% of colorectal cancer cases are sporadic and arising in individuals without significant hereditary risk (9, 29, 30). These underlying factors align with a basic principle of medicine and public health introduced by Virchow, which states that epidemics and rapid increases in rates of disease are due to disturbances of human culture (33). This suggests that efforts to increase the prevalence of protective lifestyle risk factors in the population will have a significant influence on lowering the rates of colon cancer and other lifestyle-based diseases (34, 35). Microsimulation modeling specifically shows this concept for colon cancer (36).

Strengths of this study include the prospective design with a large, non-Western population, high participant response rate, detailed collection of data through face-to-face interview, and a very low percentage of participants lost to follow-up. Others include the comprehensive assessment of mortality and cancer incidence (4). A limitation of this study is the use of self-reported lifestyle data, which may result in nondifferential misclassification and residual confounding and lead to an underestimation of the associations. We also did not have information on colorectal cancer screening practices among cohort participants.

In essence, an increasing level of protective lifestyle factors in Chinese men and women is associated with a marked decrease in rates and risk of incident colon cancer and thus overall colorectal cancer. This study highlights that multiple potentially modifiable lifestyle factors, which are generally coupled with prevention of cardiovascular disease (35), are also central for prevention of colon cancer in this population.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: A.O. Odegaard, J.-M. Yuan
Development of methodology: A.O. Odegaard, W.-P. Koh, J.-M. Yuan
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): W.-P. Koh, J.-M. Yuan
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): A.O. Odegaard, J.-M. Yuan
Writing, review, and/or revision of the manuscript: A.O. Odegaard, W.-P. Koh, J.-M. Yuan
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): J.-M. Yuan
Study supervision: J.-M. Yuan

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